

Emergence of OXA-Type Extended-Spectrum β -Lactamases Among *Enterobacter cloacae* Isolates Collected From Hospitals of Tehran, Karaj and Qazvin, Iran

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Background: Extended-Spectrum β -Lactamases (ESBLs)-producing *Enterobacter cloacae* has been increasingly reported as a major clinical concern in recent years. TEM and SHV β -lactamase are the most common ESBL genotypes that are found in Enterobacteriaceae; however, there are also new families of ESBLs, including OXA-type enzymes, which are one of the most important mechanisms of resistance to oxyimino-cephalosporin antibiotics. OXA-type ESBLs are divided into five groups.

Objectives: The main aim of the present study was to determine the frequency of *bla*_{OXA} genes among ESBL-producing *E. cloacae* isolates in three distinct provinces of Iran.

Patients and Methods: A total of 82 non-repetitive ESBL-producing *E. cloacae* isolates were collected from hospitalized patient in Qazvin, Karaj, and Tehran hospitals, Iran. The isolates were identified by standard laboratory methods and then confirmed by API 20E strips. PCR and sequencing was performed for detection of *bla*_{OXA-1}, *bla*_{OXA-2}, *bla*_{OXA-9}, and *bla*_{OXA-10} genes. The clonal relatedness of OXA-producing isolates was assessed by enterobacterial repetitive intergenic consensus PCR (ERIC-PCR).

Results: In total, 48 ESBL-producing isolates (58.5%) were positive for the *bla*_{OXA-1} gene. All *bla*_{OXA-1}-producing isolates showed multidrug resistant pattern. In this study, *bla*_{OXA-2}, *bla*_{OXA-9}, and *bla*_{OXA-10} genes were not detected. The ERIC-PCR results showed that 42 OXA-producing isolates (77.7%) were genetically diverse with different band patterns.

Conclusions: This study was the first report of the emergence of the plasmid-encoded *bla*_{OXA} genes among *E. cloacae* isolates in Iran. These findings highlight the need to use appropriate infection control policy and rational antibiotic therapy to reduce further spread of these resistant bacteria in the studied hospitals.

Keywords: *Enterobacter cloacae*; Extended-Spectrum β -Lactamases; OXA-type β -Lactamase

1. Background

Enterobacter cloacae is the most frequent bacterial that causes nosocomial infections among hospitalized patients (1, 2). This organism can cause several clinical diseases such as bacteremia as well as lower respiratory tract, skin, urinary tract, and soft-tissue infections (2). Risk factors associated with infections with *E. cloacae* include immunosuppression, long-term hospitalization, and invasive procedures or surgeries (3). Infection with *E. cloacae* is associated with increased morbidity and mortality in hospitalized patients, especially in intensive care units (ICUs) and other high-risk hospital settings (4). Beta-lactam compounds are important group of prescribed antibiotics for treatment of patients infected with *E. cloacae* (2); however, extensive and inappropriate use of broad-spectrum β -lactam antibiotics lead to appearance of multidrug resistant *E. cloacae* isolates, which severely limit the therapeutic options for treatment of infected patients. Although resistance

of *Enterobacter* species to third-generation cephalosporins is most typically caused by overproduction of AmpC β -lactamases, the role of extended-spectrum β -Lactamases (ESBLs) has been increasingly reported among Enterobacteriaceae (5). ESBLs have been found mostly in *Klebsiella* species and *Escherichia coli* but have also been described in other Enterobacteriaceae including *Enterobacter*, *Citrobacter*, and *Serratia* species. ESBLs are the most important mechanisms of resistance to third-generation cephalosporins with remarkable ability to develop resistance to several classes of antimicrobial agents (6). These enzymes have been commonly located on plasmids that are transferable from strain to strain and between bacterial species. TEM and SHV are the most common types of ESBLs among *E. cloacae* (7); however, a number of different ESBL types have been recently identified in *Enterobacter* species such as CTX-M and OXA (8). There are five groups of OXA-type ESBLs.